AB 34 33. (NEW) The microparticle according to claim 7, wherein the bronchodilator is albuterol.--

REMARKS

The claims are amended to place them in conformance with standard U.S. patent practice and idiomatic English, and to remove multiple dependencies. The support for the amendments is found in the originally filed claims, and no new matter is added.

If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: May 8, 2002

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APPENDIX TO AMENDMENT

The claims are amended as follows:

1. (ONCE AMENDED) A biocompatible microparticle [intended to be inhaled] for inhalation, comprising at least one active principle and at least one layer coating this active principle, which is [the] an external layer of said microparticle, said external layer containing at least one coating agent, [characterized in that] wherein said microparticle has a mean diameter of between 1 μm and 30 μm and an apparent density of between 0.02 g/cm^3 and 0.8 g/cm^3[, and in that it is possible for it to be obtained according to a method comprising the essential steps which are bringing together a coating agent and an active principle and introducing a supercritical fluid, with stirring in a closed reactor].

2. (ONCE AMENDED) The microparticle as claimed in claim 1, [characterized in that it has] having a mean diameter of between 1 μm and 15 μm[, and even more preferably of between 2 μm and 10 μm], and an apparent density of between 0.05 g/cm^3 and 0.4 g/cm^3, and [in that] wherein the active principle/coating agent mass ratio of this particle is between 95/5 and 5/95.

3. The microparticle as claimed in claim 1 [or 2], [which can be] obtained using a method comprising [the following steps]:

- suspending an active principle in a solution of at least one substantially polar coating agent in an organic solvent, wherein said active principle [being] is insoluble in the organic solvent, said substantially polar coating agent [being] is insoluble in a fluid in [the] a supercritical state, and said organic solvent [being] is soluble in a fluid in [the] a supercritical state,

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- bringing the suspension into contact with a fluid in [the] a supercritical state, so as to desolvate in a controlled way the substantially polar coating agent and ensure its coacervation;

- substantially extracting the solvent using a fluid in [the] a supercritical state and discharging the [SC] supercritical fluid/solvent mixture, and

- recovering the microparticles.

4. The microparticle as claimed in claim 1 [or 2], [which can be] obtained by [using] a method [which consists in] comprising:

suspending an active principle in a supercritical fluid containing at least one coating agent dissolved therein, and then in ensuring [the] coacervation of the particles by physicochemical modification of the environment.

5. The microparticle as claimed in claim 3, [characterized in that] wherein the coating agent is chosen from [the group made up of]:

- biodegradable (co)polymers of α-hydroxycarboxylic acids[, in particular homopolymers and copolymers of lactic acid and glycolic acid, and more particularly PLAs (poly-L-lactide) and PLGAs (poly(lactic-co-glycolic acid))],

- amphiphilic block polymers of [the] a poly(lactic acid)-poly(ethylene oxide) type,

- biocompatible polymers of [the] a poly(ethylene glycol), poly(ethylene oxide) type,

- polyanhydrides, poly(ortho esters), poly-ε-caprolactones, and derivatives thereof,

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- poly(β-hydroxybutyrate), poly(hydroxyvalerate), and poly(β-hydroxybutyrate-hydroxyvalerate) copolymers,
- poly(malic acid),
- polyphosphazenes,
- block copolymers of [the] a poly(ethylene oxide)-poly(propylene oxide) type,
- poly(amino acids),
- polysaccharides,
- phospholipids [such as phosphatidyl glycerols, diphosphatidyl glycerols containing C12 to C18 fatty acid chains (DLPG, DMPG, DPPG, DSPG), phosphatidylcholines, diphosphatidylcholines containing C12 to C18 fatty acid chains (DLPC, DMPC, DPPC, DSPC), diphosphatidylethanolamines containing C12 to C18 fatty acid chains (DLPE, DMPE, DPPE, DSPE), diphosphatidylserine containing C12 to C18 chains (DLPS, DMPS, DPPS, DSPS), and mixtures which contain the phospholipids mentioned],
- fatty acid esters [such as glyceryl stearates, glyceryl laurate, cetyl palmitate, or mixtures which contain these compounds], and
- mixtures [which contain] of the abovementioned compounds.

6. The microparticle as claimed in claim 4, [characterized in that] wherein the coating agent is chosen from [the group made up of]:

- phospholipids [such as phosphatidyl glycerols, diphosphatidyl glycerols containing C12 to C18 fatty acid chains (DLPG, DMPG, DPPG, DSPG), phosphatidylcholines, diphosphatidylcholines containing C12 to C18 fatty acid chains

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(DLPC, DMPC, DPPC, DSPC), diphosphatidylethanolamines containing C12 to C18 fatty acid chains (DLPE, DMPE, DPPE, DSPE), diphosphatidylserine containing C12 to C18 chains (DLPS, DMPS, DPPS, DSPS), and mixtures which contain the phospholipids mentioned],

- mono-, di-, and triglycerides in which the fatty acid chains range from C4 to C22, and mixtures [containing them] thereof,

- mixtures of glycerides and of esters of polyethylene glycol,

- cholesterol,

- fatty acid esters [such as glyceryl stearates, glyceryl laurate or cetyl palmitate],

- biodegradable or bioerodible polymers soluble in a supercritical fluid, and

- mixtures [which contain the abovementioned compounds] thereof.

7. The microparticle as claimed in [any one of claims] claim 1 [to 6], [characterized in that] wherein the active principle is chosen from [the group made up of] proteins [and], peptides[, such as insulin, calcitonin, or analogues of the hormone LH-RH], polysaccharides [such as heparin], anti-asthmatic agents, [such as budesonide, beclometasone dipropionate and its active metabolite beclometasone 17-monopropionate], beta-estradiol hormones, testosterone, bronchodilators [such as albuterol], cytotoxic agents, corticoids, antigens, and DNA fragments.

8. The microparticle as claimed in claim 2, [characterized in that] wherein the microparticle is an immediate-release microparticle, and [that] wherein the active principle/coating agent mass ratio of this particle is between 95/5 and 80/20.

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9. A method for preparing microparticles [intended to be inhaled] for inhalation, [and] comprising [the following steps]:

- suspending an active principle in a solution of at least one substantially polar coating agent in an organic solvent, wherein said active principle [being] is insoluble in the organic solvent, said substantially polar coating agent [being] is insoluble in a fluid in the supercritical state, and said organic solvent [being] is soluble in a fluid in the supercritical state,

- bringing the suspension into contact with a fluid in the supercritical state, so as to desolvate in a controlled way the substantially polar coating agent and ensure its coacervation,

- substantially extracting the solvent using a fluid in the supercritical state, and discharging the SC fluid/solvent mixture, and

- recovering the microparticles.

10. A method for preparing microparticles [intended to be inhaled] for inhalation, [which consists in] comprising suspending, with stirring, in a closed reactor, an active principle in a supercritical fluid containing at least one coating agent dissolved therein, and then in ensuring [the] coacervation of the particles by physicochemical modification of the environment.

11. (NEW) The microparticle according to claim 1, obtained according to a method comprising:

- bringing together a coating agent and an active principle; and

- introducing a supercritical fluid, with stirring, in a closed reactor.

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12. (NEW) The microparticle according to claim 2, having a mean diameter of between 2 μm and 10 μm.

13. (NEW) The microparticle according to claim 7, wherein the protein or peptide is chosen from insulin, calcitonin, and analogues of LH-RH.

14. (NEW) The microparticle according to claim 7, wherein the polysaccharide is heparin.

15. (NEW) The microparticle according to claim 7, wherein the anti-asmatic agents are chosen from budesonide, beclometasone dipropionate, and beclometasone 17-monopropionate.

16. (NEW) The microparticle according to claim 7, wherein the bronchodilator is albuterol.

17. (NEW) The microparticle according to claim 5, wherein the biodegradable (co)polymers of α-hydroxycarboxylic acids are selected from homopolymers and copolymers of lactic acid and glycolic acid.

18. (NEW) The microparticle according to claim 17, wherein the biodegradable (co)polymers of α-hydroxycarboxylic acids are selected from poly-L-lactides and poly(lactic-co-glycolic acids).

19. (NEW) The microparticle according to claim 5, wherein the phospholipids are chosen from phosphatidylglycerols, diphosphatidylglycerols containing C12 to C18 fatty acid chains, phosphatidylcholines, diphosphatidylcholines containing C12 to C18 fatty acid chains, diphosphatidylethanolamines containing C12 to C18 fatty acid chains, and diphosphatidylserines containing C12 to C18 chains.

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20. (NEW) The microparticle according to claim 19, wherein the diphosphatidylglycerols containing C12 to C18 fatty acid chains are chosen from dilauroylphosphatidylglycerol (DLPG), dimyristoylphosphatidylglycerol (DMPG), dipalmitoylphosphatidylglycerol (DPPG), and distearoylphosphatidylglycerol (DSPG).

21. (NEW) The microparticle according to claim 19, wherein the diphosphatidylcholines containing C12 to C18 fatty acid chains are chosen from dilauroylphosphatidylcholine (DLPC), dimyristoylphosphatidylcholine (DMPC), dipalmitoylphosphatidylcholine (DPPC), and distearoylphosphatidylcholine (DSPC).

22. (NEW) The microparticle according to claim 19, wherein the diphosphatidylethanolamines containing C12 to C18 fatty acid chains are chosen from dilauroylphosphatidylethanolamine (DLPE), dimyristoylphosphatidylethanolamine (DMPE), dipalmitoylphosphatidylethanolamine (DPPE), and distearoylphosphatidylethanolamine (DSPE).

23. (NEW) The microparticle according to claim 19, wherein the diphosphatidylserine containing C12 to C18 chains are chosen from dilauroylphosphatidylserine (DLPS), dimyristoylphosphatidylserine (DMPS), dipalmitoylphosphatidylserine (DPPS), and distearoylphosphatidylserine (DSPS).

24. (NEW) The microparticle according to claim 5, wherein the fatty acid esters are chosen from glycerylstearate, glyceryllaurate, cetylpalmitate, and mixtures thereof.

25. (NEW) The microparticle according to claim 6, wherein the phospholipids are chosen from phosphatidylglycerols, diphosphatidylglycerols containing C12 to C18 fatty acid chains, phosphatidylcholines, diphosphatidylcholines containing C12 to C18

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fatty acid chains, diphosphatidylethanolamines containing C12 to C18 fatty acid chains, diphosphatidylserine containing C12 to C18 chains, and mixtures thereof.

26. (NEW) The microparticle according to claim 25, wherein the diphosphatidylglycerols containing C12 to C18 fatty acid chains are chosen from dilauroylphosphatidylglycerol (DLPG), dimyristoylphosphatidylglycerol (DMPG), dipalmitoylphosphatidylglycerol (DPPG), and distearoylphosphatidylglycerol (DSPG).

26. (NEW) The microparticle according to claim 25, wherein the diphosphatidylcholines containing C12 to C18 fatty acid chains are chosen from dilauroylphosphatidylcholine (DLPC), dimyristoylphosphatidylcholine (DMPC), dipalmitoylphosphatidylcholine (DPPC), and distearoylphosphatidylcholine (DSPC).

27. (NEW) The microparticle according to claim 25, wherein the diphosphatidylethanolamines containing C12 to C18 fatty acid chains are chosen from dilauroylphosphatidylethanolamine (DLPE), dimyristoylphosphatidylethanolamine (DMPE), dipalmitoylphosphatidylethanolamine (DPPE), and distearoylphosphatidylethanolamine (DSPE).

28. (NEW) The microparticle according to claim 25, wherein the diphosphatidylserine containing C12 to C18 chains are chosen from dilauroylphosphatidylserine (DLPS), dimyristoylphosphatidylserine (DMPS), dipalmitoylphosphatidylserine (DPPS), and distearoylphosphatidylserine (DSPS).

29. (NEW) The microparticle according to claim 6, wherein the fatty acid esters are chosen from glycerylstearate, glyceryllaurate, and cetylpalmitate.

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30. (NEW) The microparticle according to claim 7, wherein the peptides are chosen from insulin, calcitonin, and analogues of luteinizing hormone-releasing hormone.

31. (NEW) The microparticle according to claim 7, wherein the polysaccharide is heparin.

32. (NEW) The microparticle according to claim 7, wherein the anti-asthmatic agent is chosen from budesonide, beclometasone dipropionate, and beclometasone 17-monopropionate.

33. (NEW) The microparticle according to claim 7, wherein the bronchodilator is albuterol.

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